March 29, 2002 in the present application. Based on these documents, it is Applicants' understanding that an earlier preliminary amendment dated Sept. 8, 2000 has been included in the file wrapper for the present continuation application. See "Decision Granting Petition and Assignment of Application Number and Notice of Omitted Items," dated Mar. 4, 2002 (page 2, para. 2, in Application No. 08/942,989, the parent application for this case). Applicants have presumed, based on the above-referenced communication, that this earlier preliminary amendment was actually entered in Continuation Application No. 09/887,706. Accordingly, we hereby cancel claims 36-63 from the prior preliminary amendment and present herein claims 64-83.

Pursuant to the Applicants' "Petition Under 37 C.F.R. §§1.17(h) and 1.181 to Accord Filing Date," filed May 28, 2002, Applicants have hereby cancelled all references to omitted drawings in the present specification. As noted in Applicants' Petition to Accord Filing Date, Applicants assert that the omitted drawings are not necessary for an understanding of the subject matter of the application under 35 U.S.C. §113. Accordingly, the amendments to the specification indicated above remove references to any drawings. No new matter is introduced by these amendments.

Claims 64-83 are now pending. Support for the new claims may be found at, for example, page 3, lines 1-34; page 3, line 34-page 4, line 5; page 10, lines 23-27; page 4, lines 19-21; page 9, lines 2-10; page 60; and pages 62-64.

Support for the chemical and physical structure of the contrast agent may be found at, for example, page 12, lines 29-34; page 14, lines 6-19; and page 18, lines 1-6. Further support for the chemical and physical structure of the SDTBM may be found at page 25, lines 6-26; and at page 27, lines 18-34 to page 28, lines 1-3. Support for the chemical structure and arrangement and positioning of the chelate, the Linker, and the SDTBM may be found at, for example, pages 39-42.

Support for the physical and chemical properties of the contrast agents may be found at page 27, lines 1-11; page 28, lines 21-34 to page 29, lines 1-16; and page 59, Example 1 and Table I.

Applicants respectfully request consideration and allowance of claims 64-83. Applicants note that according to the "Decision Granting Petition," the Office records should indicate that $547.00 in filing fees ($345.00 basic filing fee, $72.00 for 8 claims in excess of 20, and $130.00 multiple dependent claim fee, for a total of $547.00) were paid on September 8, 2000 for the present application (09/887,706).[1] Applicants respectfully point out that the preliminary amendment dated September 8, 2000 contained 54 claims in total, given the multiple dependent nature of a number of the claims. Given Applicants' presumption that the prior preliminary amendment was entered, Applicants suggest that the fee paid should have been $781.00. Applicants herein enclose a check for the balance of $234.00. If Applicants' calculation is incorrect, please apply the charge or credit to Deposit Account No. 06-1050. Applicants further note that with this supplemental preliminary amendment and the cancellation of all previously pending claims, there are presently 20 claims pending.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made."**

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 7/2/02

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[1] See "Decision Granting Petition and Assignment of Application Number and Notice of Omitted Items," dated Mar. 4, 2002 (page 3, para. 2, in Application No. 08/942,989, the parent application for this case).

Version with markings to show changes made

In the specification:

Related application data has been added.

Brief description of the drawings has been deleted.

Paragraphs entitled "Brief Description of the Drawings" which begin on page 9, line 28 and continue to page 10, line 6 have been amended as follows:

~~Brief Description of the Drawings~~

~~FIG. 1 is a graphical representation of experimental data of the effects that changes in temperature have on the observed relaxivity (R_1) for HSA solutions with and without using a contrast agent.~~

~~FIG. 2 is a graphical representation of experimental data of the loss in ROI signal intensity over time for MRI images generated using HSA solutions with and without a contrast agent.~~

~~FIG. 3 is a graphical representation of experimental data of the effects that changes in ethanol concentration have on the observed relaxivity (R_1) for HSA solutions with and without contrast agents.~~

Paragraph beginning at page 58, line 7 has been amended as follows:

The three samples were then used to monitor the thermal denaturation of the 4.5% HSA solutions. To do this, T_1 data (and thus R_1 data ($=1/T_1$)) for each sample was collected at 20 MHz over a temperature range of 20-60°C. Each sample was then removed from the NMR and heated at 85°C for 15 minutes to induce thermal denaturation of the HSA. Subsequently, the sample was returned to the NMR and T_1 data was collected at this higher temperature. See Table 1 below ~~and Figure 1~~.

Paragraph beginning at page 59, line 19 has been amended as follows:

As Table 1 ~~and Figure 1~~ shows, after thermal denaturation of the three HSA-containing solutions, the sample that also contained the HSA-specific contrast agent MS-325 demonstrated a significant decreased in the observed R_1 (a loss of 26.7 mM^{-1} sec^{-1}) during denaturation of the HSA as measured from immediately before denaturation (56.2°C) to immediately after denaturation (85°C). However, the sample that contained the non-specific contrast agent Gd-DTPA, even at a concentration of three times that used for the MS-325 sample, showed little change in R_1 (a loss of only 0.1 mM^{-1} sec^{-1}) during denaturation. This indicates that Gd-DTPA does not bind to either native or denatured HSA.

Paragraph beginning at page 60, line 24 has been amended as follows:

The phantoms were then heated in a circulating water bath with additional T_1-weighted MRI scans obtained over time. As the temperature increased, the phantoms containing MS-325 remained much brighter (less signal intensity loss as measured in % ROI (region of interest)) than the phantoms containing Gd-DTPA or 4.5% HAS alone. See Table 2 below ~~and Figure 2~~.

Paragraph beginning at page 61, line 15 has been amended as follows:

As the phantoms were heated above 50-60°C, they became opaque in color, corresponding to the thermal denaturation of the HSA. At the same time, as Table 2 ~~and Figure 2~~ shows, a dramatic loss of signal intensity was observed for the phantom that contained MS-325 (76% loss in intensity). However, the phantoms that contained Gd-DTPA or HSA alone, produced only a modest change in signal intensity. The Gd-DTPA phantoms, even at a Gd-DTPA concentration that was three times that used for the MS-325 phantoms remained as constant dark images during the MRI scans after thermal denaturation.

Paragraph beginning at page 62, line 20 has been amended as follows:

Absolute ethanol was then titrated to each of the samples. T_1 data (and thus R_1 data ($=1/T_1$)) was collected at 20 MHz and 37°C after each addition of ethanol. See Table 3 below ~~and Figure 3~~.

Paragraph beginning at page 63, line 28 continuing to page 64, line 5 has been amended as follows:

As Table 3 ~~and Figure 3~~ demonstrates, during ethanol ablation of the 4.5% HSA solutions, the sample containing MS-325 showed a significant decrease in the observed relaxivity (33 mM^{-1} sec^{-1}) and thus, allowing for the detection of ethanol induced necrosis. However, the sample containing Gd-DTPA (even at almost four times the concentration of MS-325) shows only a minor change in observed relaxivity (0.3 mM^{-1} sec^{-1}).

In the claims:

Claims 36-63 have been cancelled.

Claims 64-83 have been added.